

WHAT IS CLAIMED IS:

1. A library of viral vectors, wherein each member of the library comprises (i) a first heterologous DNA encoding a first gene product, wherein the first heterologous DNA is common to each member of the library of viral vectors, and (ii) a second heterologous DNA encoding an second gene product, wherein the second heterologous DNA varies between the members of the library of viral vectors.

2. The library of claim 1, wherein the viral vectors are adenoviral vectors.

3. The library of claim 1, wherein the first heterologous DNA and/or the second heterologous DNA is operably linked to an inducible promoter.

4. The library of claim 1, wherein the first heterologous DNA and the second heterologous DNA are under the control of separate regulatory elements.

5. The library of claim 1, wherein the first heterologous DNA and the second heterologous DNA are under the control of a bi-directional promoter.

6. The library of claim 1, wherein the first gene product is selected from the group consisting of an angiogenic factor, an anti-angiogenic factor, a transcription factor, a growth factor, a cytokine, an apoptotic agent, an anti-apoptotic agent, and a neurotrophic factor.

7. The library of claim 6, wherein said angiogenic factor is selected from the group consisting of an endothelial mitogen, a factor associated with endothelial cell migration, a factor associated with vessel wall maturation, a factor associated with vessel wall dilation, and a factor associated with extracellular matrix degradation.

8. The library of claim 1, wherein the first gene product is a kinase or a phosphatase.

9. The library of claim 1, wherein the first gene product is a vascular endothelial growth factor (VEGF).

10. The library of claim 1, wherein the first gene product is pigment epithelium-derived factor (PEDF)

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11. The library of claim 1, wherein the first gene product is fused to an antibody tag.

12. The library of claim 1, wherein the second gene product is fused to an activation domain, and the first gene product is fused to a DNA binding domain.

13. A method of identifying functionally related coding sequences, wherein the method comprises:

(a) culturing a library of viral vectors, wherein each member of the library comprises (i) a first heterologous DNA encoding a first gene product, wherein the first DNA is common to each member of the library of viral vectors, and (ii) a second heterologous DNA encoding an second gene product, wherein the second DNA varies between the members of the library of viral vectors, and

(b) comparing the activity of the gene products encoded by the library of viral vectors with the activity of the first gene product encoded by a viral vector comprising the first heterologous DNA but not comprising the second heterologous DNA.

14. The method of claim 13, wherein the viral vectors are adenoviral vectors.

15. The method of claim 13, wherein the method further comprises recovering and/or identifying the second heterologous DNA.

16. A method of constructing a library of viral vectors, wherein the method comprises:

(a) carrying out homologous recombination between a first DNA molecule and a second DNA molecule, wherein the second DNA molecule is a recipient DNA molecule comprising at least a terminal repeat and a packaging signal of a viral genome, to produce a homologously recombined pool of intermediate viral genomes, wherein the pool of intermediate viral genomes comprises double-stranded DNA,

(b) ligating one or more linear third DNA molecules into the pool of intermediate viral genomes to produce a library of viral vector genomes, wherein one or more linear third DNA molecules encodes a potentially desirable feature, and

(c) transducing the library of viral vector genomes into a first population of host cells to convert the library of viral vector genomes into a library of viral vectors.

17. The method of claim 16, wherein the second DNA molecule comprises a viral genome.
18. The method of claim 17, wherein the first DNA molecule comprises an expression cassette backbone.
19. The method of claim 18, wherein the second DNA molecule further comprises an origin of replication, an independent positive selection marker gene, and a dual selection cassette, wherein the dual selection cassette encodes a positive selection gene product and a negative selection gene product.
20. The method of claim 18, wherein the recipient DNA molecules further comprise a phage packaging site.
21. The method of claim 20, wherein the method further comprises packaging the library of viral vector genomes into phage capsids *in vitro* prior to converting the library of viral vector genomes into a library of viral vectors.
22. The method of claim 18, wherein the desirable feature is a peptide with at least one desirable activity.
23. The method of claim 18, wherein the viral vectors are adenoviral vectors.
24. The method of claim 23, wherein the method further comprises selecting an adenoviral vector comprising a desirable feature.
25. The method of claim 24, wherein selecting an adenoviral vector comprising a desirable feature comprises isolating the library of adenoviral vectors from the first population of host cells and transducing one or more populations of cells with the library of adenoviral vectors.
26. The method of claim 24, wherein selecting an adenoviral vector comprising a desirable feature comprises isolating the library of adenoviral vectors from the first population of host cells and administering the library of adenoviral vectors to an animal.
27. The method of claim 26, wherein the method comprises administering different single adenoviral vector clones to different individual animals.

28. The method of claim 23, wherein the method further comprises identifying the linear DNA molecule encoding the desirable feature.

29. The method of claim 24, wherein the desirable feature is a therapeutic peptide.

30. The method of claim 29, wherein the therapeutic peptide is an angiogenic peptide, and selecting the adenoviral vector comprising a desirable feature comprises detecting neovascularization in the animal.

31. The method of claim 18, wherein two or more linear DNA molecules are incorporated into the recipient DNA molecules.

32. The method of claim 18, wherein the recipient DNA molecules further comprise at least one nucleic acid sequence encoding a gene product other than that encoded by the linear DNA molecule, wherein the nucleic acid sequence is common to each member of the library of adenoviral vectors.

33. The method of claim 32, wherein the gene product is a VEGF.

34. The method of claim 32, wherein the gene product is PEDF.

35. The method of claim 18, wherein the library of viral vectors is co-administered with an expression vector comprising at least one nucleic acid sequence encoding a gene product other than that encoded by the linear DNA molecule.

36. A method of constructing a library of viral vectors, wherein the method comprises:

(a) providing (i) linear DNA molecules, wherein one or more linear DNA molecules encodes a potentially desirable feature, and (ii) recipient DNA molecules comprising at least a terminal repeat and a packaging signal of viral genome, an origin of replication, an independent positive selection marker gene, and a dual selection cassette, wherein the dual selection cassette encodes a positive selection gene product and a negative selection gene product,

(b) carrying out homologous recombination between the linear DNA molecules and the recipient DNA molecules to produce a homologously recombined library of viral

vector genomes, wherein the library of viral vector genomes comprises double-stranded DNA,

(c) propagating the homologously recombined library of viral vector genomes under conditions wherein the negative selection gene product is active to obtain a selected DNA, and

(d) transducing the library of viral vector genomes into a first population of host cells to convert the library of adenoviral vector genomes into a library of viral vectors.

37. The method of claim 36, wherein the recipient DNA molecule comprises a viral genome.

38. The method of claim 37, wherein the recipient DNA molecules further comprise a phage packaging site.

39. The method of claim 38, wherein the method further comprises packaging the library of viral vector genomes into phage capsids *in vitro* prior to converting the library of viral vector genomes into a library of viral vectors.

40. The method of claim 37, wherein the desirable feature is a peptide with at least one desirable activity.

41. The method of claim 37, wherein the viral vectors are adenoviral vectors.

42. The method of claim 41, wherein the method further comprises selecting an adenoviral vector comprising a desirable feature.

43. The method of claim 42, wherein selecting an adenoviral vector comprising a desirable feature comprises isolating the library of adenoviral vectors from the first population of host cells and transducing one or more populations of cells with the library of adenoviral vectors.

44. The method of claim 42, wherein selecting an adenoviral vector comprising a desirable feature comprises isolating the library of adenoviral vectors from the first population of host cells and administering the library of adenoviral vectors to an animal.

45. The method of claim 44, wherein the method comprises administering different single adenoviral vector clones to different individual animals.

46. The method of claim 41, wherein the method further comprises identifying the DNA fragment encoding the desirable feature.

47. The method of claim 42, wherein the desirable feature is a therapeutic peptide.

48. The method of claim 47, wherein the therapeutic peptide is an angiogenic peptide, and selecting the adenoviral vector comprising a desirable feature comprises detecting neovascularization in the animal.

49. The method of claim 37, wherein two or more linear DNA molecules are incorporated into the recipient DNA molecules.

50. The method of claim 37, wherein the recipient DNA molecules further comprise at least one nucleic acid sequence encoding a gene product other than that encoded by the linear DNA molecule, wherein the nucleic acid sequence is common to each member of the library of adenoviral vectors.

51. The method of claim 50, wherein the gene product is a VEGF.

52. The method of claim 50, wherein the gene product is PEDF.

53. The method of claim 37, wherein the library of viral vectors is co-administered with an expression vector comprising at least one nucleic acid sequence encoding a gene product other than that encoded by the linear DNA molecule.

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